

METHODS AND COMPOSITIONS FOR THE DIFFERENTIATION OF  
HUMAN PREADIPOCYTES INTO ADIPOCYTES

ABSTRACT OF THE DISCLOSURE

The present invention provides methods and compositions for the consistent and quantitative differentiation of human preadipocytes isolated from adipose tissue into adipocytes bearing biochemical, genetic, and physiological characteristics similar to that observed in isolated primary adipocytes. The methods of the invention comprise incubating isolated human preadipocytes, plated at least about 25,000 cells/cm<sup>2</sup>, in a medium containing, glucose, a cyclic AMP inducer such as isobutylmethylxanthine or forskolin, a glucocorticoid or glucocorticoid analogue, insulin or an insulin analogue and a PPAR $\gamma$  agonist or a RXR agonist. The compositions of the invention include media for the differentiation of human preadipocytes, human adipocytes differentiated by the methods of the invention and transfected adipocytes.

The present invention also provides methods for determining the ability of a compound to affect the differentiation of human preadipocytes to adipocytes, for determining the ability of a compound to act as a PPAR $\gamma$  antagonist, a glucocorticoid, a glucocorticoid analogue, or an insulin analogue, for transfecting cultured human adipocytes, and as a means to identify novel polypeptides secreted from human adipocytes into the conditioned medium. The methods and compositions have use in the drug discovery of compounds having relevance to the disease states of diabetes, obesity, and cardiovascular disease and in the studies of these diseases.